Case Report Rapport de cas

Multiple session mesotherapy for management of coxofemoral osteoarthritis pain in 10 working dogs: A case series

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Abstract — The aim of this study was to document the effects of mesotherapy in working dogs diagnosed with hip osteoarthritis (OA) and related pain. Ten police working dogs with hip OA and related pain were treated with a combination of lidocaine, piroxicam, and thiocolchicoside, injected in multiple intradermal points. Seven treatment sessions were conducted. The Canine Brief Pain Inventory (CBPI) and the Hudson Visual Analogue Scale (HVAS) were used in the assessment of response to treatment compared to evaluation before treatment (T0), after 15 d, 30 d, 60 d, 90 d, 120 d, 150 d, and 180 d after initial treatment. Results were compared using the Wilcoxon signed-rank test.

Significant differences were experienced in CBPI scores comparing moments with T0: at 15 d ($P = 0.03$ for Pain Interference Score — PIS) and $P = 0.02$ for Pain Severity Score — PSS), 30 d ($P < 0.05$ for PIS and $P < 0.05$ for PSS), 60 d ($P = 0.04$ for PIS and $P = 0.01$ for PSS) and 180 d ($P = 0.04$ for PSS). Individual treatment results were considered successful in 40% of animals at 15 d and 30 d, 66.7% at 60 d, 44% at 90 d, 37.5% at 120 d, and 25% at 150 d. The HVAS scores showed no significant differences.

Mesotherapy may be an option for the treatment of canine musculoskeletal-related pain. Further studies are required.

Résumé — Mésothérapie en plusieurs séances pour la prise en charge de la douleur arthrosique coxofémorale chez 10 chiens de travail : une série de cas. Le but de cette étude était de documenter les effets de la mésothérapie chez les chiens de travail diagnostiqués avec une arthrose de la hanche (OA) et des douleurs associées. Dix chiens de travail policiers souffrant d'OA et de douleurs associées ont été traités avec une combinaison de lidocaïne, de piroxicam et de thiocolchicoside, injectée en plusieurs points intradermiques. Sept séances de traitement ont été réalisées. Le *Canine Brief Pain Inventory* (CBPI) et l'échelle visuelle analogique de Hudson (HVAS) ont été utilisés dans l'évaluation de la réponse au traitement par rapport à l'évaluation avant traitement (T0), après 15 j, 30 j, 60 j, 90 j, 120 j, 150 j et 180 j après le traitement initial. Les résultats ont été comparés à l'aide du test des rangs signés de Wilcoxon.

Des différences significatives ont été observées dans les scores CBPI comparant les moments avec T0 : à 15 jours ($P = 0{,}03$ pour *Pain Interference Score* – PIS) et $P = 0{,}02$ pour *Pain Severity Score* – PSS), 30 jours ($P < 0{,}05$ pour PIS et $P < 0{,}05$ pour PSS), 60 jours ($P = 0{,}04$ pour PIS et $P = 0{,}01$ pour PSS) et 180 jours ($P = 0{,}04$ pour PSS). Les résultats du traitement individuel ont été considérés comme réussis chez 40 % des animaux à 15 jours et 30 jours, 66,7 % à 60 jours, 44 % à 90 jours, 37,5 % à 120 jours et 25 % à 150 jours. Les scores HVAS n'ont montré aucune différence significative.

La mésothérapie peut être une option pour le traitement des douleurs musculosquelettiques canines. Des études complémentaires sont nécessaires.

(Traduit par Dr Serge Messier)

Can Vet J 2022;63:597–602

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Introduction

Osteoarthritis (OA) affects all animals (1,2). It has an estimated prevalence of 20% in dogs, particularly working dogs with high physical demands. The most common and relevant clinical sign, and a hallmark of the disease, is chronic pain (3–5). Prevalence of this condition is expected to increase due to a simultaneous increase in life expectancy and obesity. In one study, OA was identified in 98% of dogs followed until their end of life (6). Osteoarthritis is incurable and challenging to treat despite being a common condition (7,8). The condition has an effect on gait, posture, activity, and overall performance in working dogs.

Mesotherapy is an administration technique in which drugs or other substances are deposited in small quantities in the dermis. From these microdeposits created in the skin over the area of the condition being treated, the drugs are slowly released to the surrounding tissues, muscles, tendons, and ligaments, which are also a source of pain in OA (9,10). Mesotherapy has a rapid onset of action, a prolonged local action, and a drug-sparing effect, having been described as superior to systemic therapy for musculoskeletal pain relief in humans (11,12). Mesotherapy has been described in the treatment of various musculoskeletal conditions, such as back pain and osteoarthritis, in humans, horses, and dogs (13–16).

Evaluation of chronic pain in animals is challenging, and can be performed by subjective and objective methods. The Canine Brief Pain Inventory (CBPI) is a questionnaire designed to assess owners' perception of the impact of chronic pain on their dog. It has been used to detect improvements in the treatment of OA in dogs receiving NSAIDs (17). The CBPI is divided into 2 components: a pain severity score (PSS) that assesses the magnitude of pain experienced by a dog, and a pain interference score (PIS) that evaluates the degree to which pain affects daily activities (18). The Hudson Visual Analogue Scale (HVAS) is a validated tool for assessing lameness in dogs (19).

This report aims to describe the use and effectiveness of mesotherapy in working dogs with hip OA-related pain.

Materials and methods

This study is a part of a project approved by the Ethical Review Group of the Association of Veterinary Anaesthetists (No. 2020-010). Written, informed consent was obtained from the Institution responsible for all the animals (Guarda Nacional Republicana, Portuguese Gendarmerie). Animals were included from the population of working dogs of the Grupo de Intervenção Cinotécnico (Portuguese Gendarmerie Canine Unit). Dogs were selected based on history, trainer complaints (difficulty rising, jumping, and maintaining obedience positions, stiffness, and decreased overall performance), physical (pain during joint mobilization, stiffness, and reduced range of motion), and radiographic findings consistent with bilateral hip OA. Dogs with other illnesses were excluded based on physical, orthopedic, and neurological examination, complete blood (cell) count, and serum chemistry profile. Animals included in the study could not be under any other treatment.

In this single-blinded study (trainers were unaware of the type of treatment their animals received), dogs were treated with a solution of 40 mg of lidocaine (Anestesin; Laboratório Sorológico, Amadora, Portugal), 20 mg of piroxicam (Feldene; Pfizer, Porto Salvo, Portugal), and 4 mg of tiocolchicoseide (Relmus; Sanofi, Porto Salvo, Portugal), based on an identical protocol used for the treatment of OA in humans (20). A total solution volume of 4 mL was prepared, regardless of the animal's weight. In each injection point, 0.1 mL was injected intradermally, using 27-G needles, 4-mm in length (Mesoram; Miami, Florida, USA). Injection sites were spaced approximately 2 cm apart (10,21), along the skin area corresponding to the location of the coxofemoral joint: laterally on a 4×4 cm area with the greater trochanter at its center, and medially on a similar-sized area, having the coxofemoral joint at the center. Thirty-five to 40 injections were done on each animal, depending on the dog's size. Injections were conducted with the needle at an average inclination of 30° at a depth of up to 4 mm (21,22). Only mild restraint and no sedation were required to conduct treatment sessions. Animals were rested for 3 d after the initial treatment session and then resumed normal activity over 5 d (16).

The assisting veterinarian examined all animals 1 and 4 d after initial treatment for any abnormal findings induced by the treatment. If none were detected, the animal was permitted to return to normal work. A total of 7 injection sessions were conducted for each animal; 4 weekly sessions followed by 3 sessions 15 d apart (21). With mesotherapy, adverse effects are extremely rare and mild, and if they occur, include nausea, vomiting, diarrhea, mild pain, edema, pruritus, and erythema (23). Signs of any possible adverse effects were recorded during the follow-up examination.

Response to treatment as measured with the CBPI and HVAS, was evaluated before treatment (T0), after 15 d (after 2 treatment sessions), 30 d (after 4 treatment sessions), 60 d (after 6 treatment sessions), 90 d (after all 7 treatment sessions), 120 d, 150 d, and 180 d after initial treatment. The trainers completed these without seeing their previous evaluation. The CBPI includes a question to classify the animals' overall quality of life, comprising 5 levels: bad, reasonable, good, very good, and excellent.

Normality was assessed with a Shapiro-Wilk test. Results of each evaluation moment were compared with those before treatment with the Wilcoxon signed ranks test. IBM SPSS Statistics version 20 was used for the statistical analysis, $P < 0.05$.

Results

Ten animals comprised the sample, representing 5 breeds, German shepherd (n = 5), Labrador retriever (n = 2), Belgian Malinois shepherd (n = 1), Dutch shepherd (n = 1), and catch dog of São Miguel Island (n = 1). Eight males and 2 females were included, with a mean weight of 32.3 kg ($\pm$ 4.9 kg) and a mean age of 6.7 y ($\pm$ 1.05 y). Of the animals enrolled, 2 had to be excluded. One was excluded due to the impossibility of medical follow-up after 30 d. Another dog was eliminated after 90 d, as he suffered a third phalanx avulsion of the second digit of the right thoracic limb. Data obtained from these animals up to the moment of exclusion was included in the analysis. The CBPI and HVAS answers were collected in all evaluation moments, up to the study's end or when an animal was excluded. The number

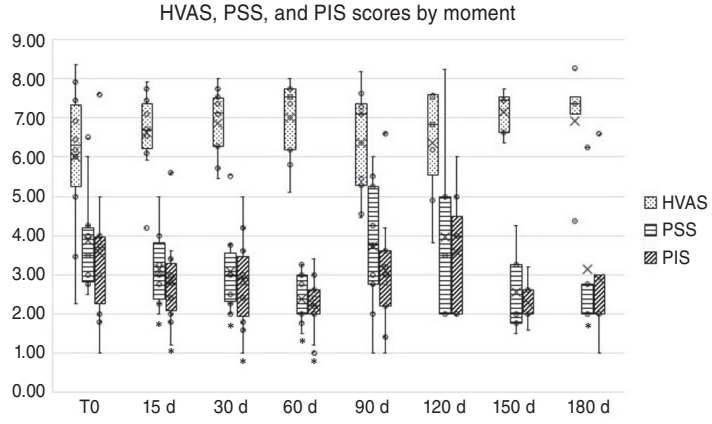

Figure 1. Overall Hudson Visual Analogue Scale (HVAS), Pain Severity Score (PSS), and Pain Interference Score (PIS) registered, by moment.
* Indicates significant variation.

of injections performed in each animal varied with its size to cover the area being injected. No adverse effects were detected.

When comparing results for each moment with T0, differences were observed at 15 d ($P = 0.03$ for PIS and $P = 0.02$ for PSS), 30 d ($P < 0.05$ for PIS and $P < 0.05$ for PSS), 60 d ($P = 0.04$ for PIS and $P = 0.01$ for PSS) and 180 d ($P = 0.04$ for PSS) (Figure 1). Individual treatment success, as measured by the CBPI, has been defined as a reduction of ≥ 1 in PSS and ≥ 2 in PIS (24). Treatment was successful in reducing PSS in 4 out of 10 animals at 15 d and 30 d (40%), 6/9 at 60 d (67%), 4/9 at 90 d (44%), 3/8 at 120 d (37.5%), 2/8 at 150 d (25%) and none at 180 d. In addition, PSS results improved for 8/10 animals at 15 d (80%), 8/9 at 60 d (88.9%), 6/9 at 90 d (67%), 4/8 at 120 d (50%) and 3/8 at 150 and 180 d (37.5%). Considering PIS, treatment was a success in 1 out of 10 animals at 15 d and 30 d (10%), 3/9 at 60 d (33.3%), 1/9 at 90 d (11.1%,), 2/8 at 120 d (25%), and 1/8 at 150 d and 180 d (12.5%). Treatment also improved PIS scores for 6/10 animals at 15 and 60 d (60%), 6/9 at 90 d (67%), 2/8 at 120 and 150 d (25%), and 1/8 at 180 d (12.5%).

No significant differences were registered in the results of the HVAS in each moment with T0 (Figure 1). When considering individual results, an improvement in results was observed in 5/10 animals at 15 d (50%), 8/10 at 30 d (80%), 7/9 at 60 d (77.7%), 5/9 at 90 d (55.6%), 3/8 at 120 d and 150 d (37.5%), and 2/8 at 180 d (25%). Mean scores for PSS, PIS, and HVAS at the various times, are presented in Table 1. Individual scores for PSS, PIS, and HVAs are presented in Tables 2, 3, and 4, respectively.

Considering trainers' classification of the quality of life at T0, 4/10 of animals were considered to have a very good quality of life, another 4/10 as good, 1/10 as reasonable, and 1/10 as bad. This distribution of classifications changed at 15 d, with 6/10 of animals classified as having a very good quality of life and 3/10 as good and 1/10 as reasonable. At 30 d and 60 d, animals were classified as having very good (5/10 and 2/9, respectively) or good (5/10 and 7/9, respectively) quality of life. At 90 d, 3/9 animals were classified as having a very good quality of life,

Table 1. Significant improvements in Pain Severity Score (PSS) and Pain Interference Score (PIS) of the Canine Brief Pain Inventory (CBPI), and improvements in HVAS scores, by moment.

	T0		T1		T2		T3		T4		T5		T6		T7	
Survey	Score	*P*-value	Score	*P*-value	Score	*P*-value	Score	*P*-value	Score	*P*-value	Score	*P*-value	Score	*P*-value	Score	*P*-value
PSS	3.9 ± 1.36	—	3.1 ± 0.93	0.02	2.9 ± 1.03	0.04	2.4 ± 0.68	0.01	3.7 ± 1.69	0.68	3.9 ± 2.33	0.49	3.1 ± 1.18	0.14	2.58 ± 1.79	0.04
PIS	3.6 ± 1.85	—	2.9 ± 1.21	0.03	2.8 ± 1.21	0.04	2.2 ± 0.77	0.04	3.1 ± 1.65	0.17	3.6 ± 1.61	0.92	2.3 ± 0.63	0.46	2.9 ± 2.17	0.28
HVAS	6.0 ± 1.93	—	6.6 ± 1.07	0.11	6.9 ± 0.86	0.07	7 ± 1.03	0.17	6.4 ± 1.42	0.59	6.3 ± 1.48	0.92	7.1 ± 0.59	0.07	6.6 ± 6.56	1

Table 2. Evolution of individual of Pain Severity Scores (PSS) and percentual variation compared with T0, by moment.

	PSS													
	T0	15		30		60		90		120		150		180	
Patient	Score	Score	%	Score	%	Score	%	Score	%	Score	%	Score	%	Score	%
1	3.5	2.0*	42.9	5.5	−57.1	2.0**	42.9	2.0**	42.9	2.0**	42.9	1.5**	57.1	2.8	20.0
2	4.3	4.0*	7.0	3.8*	11.6	3.3**	23.3	5.5	−27.9	5.0	−16.3	4.3	0.0	4.3	0.0
3	2.8	3.3	−17.9	2.3*	17.9	2.0*	28.6	1.0**	64.3	2.0**	28.6	1.8**	35.7	2.0*	28.6
4	2.8	2.0*	28.6	2.0*	28.6	2.8	0.0	4.3	−53.6	2.0*	28.6	2.0*	28.6	2.0*	28.6
5	2.5	2.8	−12.0	2.5	0.0	1.5**	40.0	2.0*	20.0	2.5	0.0	2.5	0.0	2.5	0.0
6	3.0	2.3*	23.3	2.0**	33.3	2.0**	33.3	2.8*	6.7	3.5	−16.7	3.3	−10.0	2.8*	6.7
7	4.0	3.0**	25.0	3.0**	25.0	—	—	—	—	—	—	—	—	—	—
8	6.5	5.0**	23.1	2.8**	56.9	3.0**	53.8	5.3**	18.5	5.0**	23.1	6.3	3.1	6.3	3.1
9	6.0	4.0**	33.3	3.0**	50.0	1.8**	70.0	3.8**	36.7	8.3	−38.3	7.0	−16.7	7.5	−25.0
10	3.5	2.3**	34.3	3.0*	14.3	3.3*	5.7	3.5	0.0	—	—	—	—	—	—

* Indicates score improvement.
** Indicates significant score improvement.

Table 3. Evolution of individual of Pain Interference Scores (PIS) and percentual variation compared with T0, by moment.

	PIS													
	T0	15		30		60		90		120		150		180	
Patient	Score	Score	%	Score	%	Score	%	Score	%	Score	%	Score	%	Score	%
1	5.0	3.4*	32.0	5.0	0.0	2.2**	56.0	2.2**	56.0	2.0**	60.0	1.6**	68.0	1.0**	80.0
2	3.6	3.6	0.0	3.6	0.0	2.6*	27.8	3.2*	11.1	4.0	−11.1	2.6*	27.8	3.6	0.0
3	1.8	1.8	0.0	2.8	−55.6	2.0	−11.1	1.0*	44.4	2.0	−11.1	2.0	−11.1	2.0	−11.1
4	2.0	2.0	0.0	1.6*	20.0	2.2	−10.0	4.2	−110.0	2.0	0.0	2.0	0.0	2.0	0.0
5	1.0	1.2	−20.0	1.0	0.0	1.0	0.0	1.4	−40.0	1.0	0.0	1.0	0.0	1.2	−20.0
6	3.0	2.4*	20.0	1.8*	40.0	2.4*	20.0	2.8*	6.7	4.0	−33.3	3.2	−6.7	3.0	0.0
7	3.8	3.0*	21.1	3.0*	21.1	—	—	—	0.0	—	—	—	—	—	—
8	7.6	5.6**	26.3	4.2**	44.7	3.4**	55.3	6.6	13.2	5.0**	34.2	6.6	13.2	6.6	13.2
9	4.0	2.8*	30.0	2.4*	40.0	1.2**	70.0	3.6*	10.0	6.0	−50.0	5.0	−25.0	5.0	−25.0
10	3.8	2.8*	26.3	3.0*	21.1	3.0*	21.1	3.8	0.0	—	—	—	—	—	—

* Indicates score improvement.
** Indicates significant score improvement.

Table 4. Evolution of individual of Hudson Visual Analogue Scale (HVAS) scores and percentual variation compared with T0, by moment.

	HVAS													
	T0	15		30		60		90		120		150		180	
Animal	Score	Score	%	Score	%	Score	%	Score	%	Score	%	Score	%	Score	%
1	8.4	7.7	−8.3	7.5	−10.7	7.4	−11.9	7.6	−9.5	7.6	−9.5	7.5	−10.7	7.4	−11.9
2	6.5	6.5	0.0	7.2	10.8	5.1	−21.5	4.5	−30.8	6.5	0.0	6.4	−1.5	6.4	−1.5
3	7.5	7.5	0.0	7.1	−5.3	7.6	1.3	7.4	−1.3	7.5	0.0	7.5	0.0	7.5	0.0
4	7.9	7.9	0.0	8.0	1.3	8.0	1.3	8.2	3.8	8.0	1.3	8.2	3.8	8.3	5.1
5	6.2	6.1	−1.6	7.4	19.4	7.5	21.0	7.3	17.7	6.2	0.0	6.2	0.0	6.0	−3.2
6	6.9	7.1	2.9	7.7	11.6	7.7	11.6	7.1	2.9	6.2	−10.1	6.6	−4.3	3.0	−56.5
7	6.0	6.7	11.7	6.3	5.0	6.0	0.0	5.5	−8.3	5.8	−3.3	6.0	0.0	5.8	−3.3
8	2.3	4.2	82.6	5.7	147.8	5.8	152.2	4.5	95.7	4.9	113.0	5.5	139.1	6.6	187.0
9	3.5	6.6	88.6	6.3	80.0	7.7	120.0	5.3	51.4	3.8	8.6	4.0	14.3	3.5	0.0
10	5.0	5.9	18.0	5.5	10.0	6.2	24.0	5.0	0.0	5.0	0.0	4.8	−4.0	4.8	−4.0

* Indicates score improvement.

4/9 as having a good quality of life, and 2/9 had a reasonable classification. From 120 d on, 4/8 had a very good quality of life, 2/8 had a good quality of life, and 2/8 had a reasonable classification.

Discussion

Osteoarthritis management focuses mainly on controlling symptoms, predominantly pain (25,26). Our results show that mesotherapy can provide significant short-term pain relief in working dogs with OA, making it an interesting tool in managing the disease. Joint pain and function are influenced by sensory innervation of all composing and surrounding tissues, such as muscle, tendons, ligaments, and remaining joint tissues (1,9). Mesotherapy targets all of these tissues. It is postulated that the applied drugs diffuse from the microdeposit to all underlying tissues, even those with poor vascularization,

reaching high concentration levels superior to those obtained with other administration routes (10).

The CBPI survey is frequently used in veterinary medicine to assess chronic pain in dogs (17,24,27,28). It has the advantage of quantifying the owner's assessment of the dog in their environment and over time. In dogs with OA, successful treatment has been set as a decrease in PSS $\geq$ 1 and PIS $\geq$ 2 (24,28). Mesotherapy significantly reduced scores of working dogs with hip OA, particularly PSS. The entirety of individual treatment sessions distributed over 10 wk, and the beneficial effects of the treatment were observed throughout this period and, for some animals, well beyond this time. Even though a significant reduction was not observed for all animals, 80% of animals showed a PSS reduction between 15 and 60 d, 55% at 90 d, 50% at 120 d, and 37.5% at 150 and 180 d (37.5%), with peak improvements being registered after the first 4 sessions, conducted once a week. This prolonged effect has been previously described (10), and it is probably due to a combination of local drug action and improved joint function resulting from the use of a less painful joint.

Results for PIS registered less significant improvements, but at 30 d, 60% of animals showed a score reduction; a value that declined up to 180 d, in which 12.5% of animals still registered better results than initial scores. Some factors may account for this fact. Since most of the treated animals showed only mild clinical signs, PIS scores were low initially, making it difficult to reduce this score significantly. In addition, as these dogs have high work motivation, they may still exhibit good performance in daily activities, leading to a low perception of pain interference. When trainers were asked to classify the animal's quality of life, all but one was seen to have very good or at least good quality of life on the first evaluation points after beginning treatment (15 d), and all up to 2 mo (60 d), this corresponding to the evaluation point in which better results were registered with the CBPI. From this point on, most animals were still considered to have a good quality of life. The fact that the animals enrolled in this study are working dogs means that their musculoskeletal structures are in greater demand compared with a companion animal. With that in mind, it is possible that results may remain evident for a longer period of time in companion animals due to the lower physical demand. On the other hand, most of the animals included in this study had only mild symptoms since signs of the disease are usually detected early, which may not be true for a companion animal. Difficulty jumping is a common complaint in working dogs; even in dogs without apparent musculoskeletal disease (29). Visual analog scales are commonly used to evaluate the severity of pain, allowing comparisons between or among analgesic regimens. The Hudson Visual Analogue Scale (HVAS) has been validated against force plate analysis (19). We did not observe significant variations in HVAS scores, even though individual results seemed to improve in almost all animals. Since visual analog scales are more sensitive in detecting and recording changes in more overt cases of lameness, and most of the animals included in the study showed only mild signs, a significant change may be harder to detect with the HVAS.

We chose a specific drug combination based on a protocol described for management of human OA (20). In addition to being described in humans, this particular drug combination seemed to make sense to address all the tissues involved in OA-related pain (1). However, other drug combinations are described (20), and their evaluation may be a topic for future research. Also, it would be interesting to evaluate the effect of a single drug compared to that of combined drugs. The effect of a single drug is hard to determine, as most described mesotherapy protocols present the combined use of different drugs (20,21), and recommendations for the use of a single drug are based on a reduced risk of drug-drug interactions and local side effects, not on the effect of the drug itself (10).

We also chose these specific evaluation moments based on previous reports on the evaluation of OA treatment in dogs (30–33). However, additional or different evaluation moments can be selected, for example, to correspond with treatments times. The selection of treatment moments can also be adjusted. We chose this protocol based on the treatment frequency suggested for human musculoskeletal pain management (21). The authors also indicate the possibility of monthly or every 15-day sessions, as needed. As this was the first description of the use of mesotherapy in the management of hip OA in working dogs, we considered it interesting to evaluate the longevity of the results. The treatment has been described as having a long-lasting effect, amounting to months in some cases (16,34). It is possible that additional sessions, 3 or 4 mo following initial treatment, would produce different outcomes. These variables and their effects, from drug selection to treatment algorithm and the effect of mesodermal modulation, must be evaluated in future studies (22). No adverse effects were observed in the animals treated. Mesotherapy can be combined with other systemic therapies and may also be an option if other therapies are not a choice due to existing comorbidities. Further studies addressing this possibility are required.

This study had some limitations, namely its sample size, the lack of a control group, and the fact that it was only single-blinded. For this study, we selected the CBPI and HVAS as outcome measures, as they have been validated for the evaluation of pain and lameness in dogs, and focus on 2 major clinical signs of OA: pain and mobility (35). Further studies should include other evaluation methods, such as other available clinical metrology instruments (the Liverpool Osteoarthritis in Dogs or the Canine Orthopedic Index). Although these scales are useful in clinical settings, they are susceptible to bias, as in the case of the caregiver placebo effect (36,37), particularly in the absence of a control group. Also, for these reasons, future studies should include objective measures, such as Force Plate Gait Analysis. Since study herein presented positive hip OA-related pain management results, future studies should enroll larger numbers of animals and a control group.

In conclusion, mesotherapy may be a treatment option in dogs with OA. In this study, it resulted in lower pain severity scores in some police working dogs with hip OA-related pain, with improvements lessening after the last treatment session. Further studies are required, with more animals, with different hip OA grades, and evaluating other medications or combinations. The present treatment algorithm is safe and adequate to treat this clinical problem. CVJ

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